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A Prospective Comparative Study of Effectiveness of 0.5% Timolol, 0.2% Brimonidine and 0.005% Latanoprost in Glaucoma Patients at a Tertiary Care Hospital.

Sampath D[1], Jyoti Upadhyay[2], Chaganti Nagesh[3],Rajesh Kumar Manchi*[4], Dr Preeti Mishra[5].

[1]Department of Pharmacology, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India.
[2]Department of Pharmacology, Prasad Institute of Medical Sciences, Sarai Shahzadi, Banthara, Lucknow-226401, Uttar Pradesh, India.
[3]Department of Pharmacology, Government Medical College, Kannauj, India. 209732
[4]Department of Pharmacology, Saraswati Medical College & Research Centre , Unnao, Uttar Pradesh, India. 209859
[5]Department of Pharmacology, Prasad Institute of Medical Sciences, Sarai Shahzadi, Banthara, Lucknow-226401, Uttar Pradesh, India.

*Address for Correspondence: Mr. Rajesh Kumar Manchi,
Email Id- manchirajesh1985@gmail.com.

ABSTRACT

Background: Timolol, brimonidine and latanoprost are three different classes of drugs used in the treatment of glaucoma. These drugs act through different mechanisms to reduce the intraocular pressure (IOP). The present study aimed to evaluate the effectiveness of timolol 0.5%, brimonidine 0.2% and latanoprost 0.005% in treatment of glaucoma.

Methods: This three arm parallel group randomized study was done at Narayana General Hospital

& Modern Eye Care Hospital, Nellore. This study included 30 patients randomly allocated to three groups 1, 2, and 3 receiving treatments with timolol 0.5%, brimonidine 0.2% and latanoprost 0.005% respectively.

Results: Total 10 patients were included in each group (1, 2, 3). The baseline characteristics were comparable between the groups. The group 1 patients showed significant decrease in IOP on day 3 of treatment, in comparison to baseline IOP. The same was observed with other groups also. In comparison of mean reduction of IOP between groups, group 3 patients showed significantly more reduction in IOP.

Conclusion: Latanoprost has shown more efficacy in comparison to timolol and brimonidine in reducing the IOP.

Keywords: Three-arm study; glaucoma; intraocular pressure.

INTRODUCTION

Glaucoma is the progressive disorder of causing optic neuropathy and second cause of permanent blindness that can be preventable. During 1996, 10% prevalence of glaucoma was seen causing bilateral blindness [1] and currently in India, its incidence is 12 million [2]. The equilibrium between the production and drainage of aqueous humor determines the intraocular pressure (IOP).

Theoretically, the normal IOP is 10-20 mm Hg, but even these pressures may be pathological [3]. Excess production of aqueous humor is the main causal factor for rise in IOP. This excess production was due to catecholamines release from adrenal medulla [4].

The β-blockers, carbonic anhydrase inhibitors, α_2-agonists and prostaglandins are the current drugs of choice for the treatment of glaucoma. Timolol is a β-blocker which increases the outflow and in long run decreases the production [3]. Brimonidine decreases aqueous humor synthesis by inhibiting adenylate cyclase enzyme and enhances aqueous drainage by regulating release of prostaglandins [5, 6]. Latanoprost is a prostaglandin analogue and enhances the drainage of aqueous humor [7]. The present study was designed to evaluate the effectiveness of 0.5% timolol,

0.2% brimonidine and 0.005% latanoprost in treatment of glaucoma.

MATERIALS AND METHODS

Thirty (30) glaucoma patients were selected for this purpose of experiment from Narayana General Hospital & Modern Eye Care Hospital, Nellore. The institutional ethics clearance and patient consent was obtained before starting the study. Patients aged between 18 - 70 years of either sex with I.O.P > 21 mm Hg and with Open angle Glaucoma (or) Ocular hypertensive's were included in the study. Patients aged between 18-70years of either sex with I.O.P > 21mm Hg and Open angle glaucoma (or) Ocular hypertension were included in the study. ~ History of hypersensitivity to any drugs used in the study. Patients with narrow angle Glaucoma or Secondary Glaucoma, any corneal abnormality that would prevent accurate LO.P reading, any uncontrollable diseases, any inflammatory conditions like conjunctivitis, keratitis, (or) uveitis, and pregnancy or breast feeding were excluded from the study.

Eligible patients underwent detailed physical examination after a detailed ophthalmic and medical history was taken. Laboratory investigations including blood sugar levels were carried out. The ophthalmic examination included measurement of visual acuity, lOP, slit lamp microscopy and dilated fundus ophthalmoscopy and visual field recorded. Thirty Glaucoma patients were randomly grouped using blind card selection method in to 3 groups, (1, 2, & 3) and each group consists of ten (10) patients. Group 1 patients received timolol (0.5%), group 2 patients received brimonidine

(0.2%) and group 3 patients received latanoprost (0.005%).

The base line LO.P was recorded for every patient with the help of Schiotz tonometer [8]. After recording the baseline LO.P, the group 1 patients received one drop of Timolol (0.5%) eye drop per a day, group 2 patients received one drop of Brimonidine (0.2%) eye drop per a day, and group 3 patients received one drop of Latanoprost (0.005%) eye drop per a day. After the

instillation of eye drop the LO.P. was measured after 30 mins. Then the patients of respective group were received with respective drug and the LO.P was measured by Schiotz tonometer, every day after instillation of the drug.

Follow-up and appointments were scheduled every month till the completion of duration of the study following the initial assessment. At subsequent visits, a complete physical examination of the eye was performed. Anti-glaucoma treatment was re - assessed based on the previous clinical examinations and patient feedback related to intolerance or side effects of current drug treatment. Any change in demographic information was recorded.

Statistical Analysis

The data was expressed as mean, standard deviation. The value of significance was obtained using ANOVA and for categorical data Chi-square test was used.

RESULTS

Details of patient are given in the CONSORT flow diagram (Figure 1). 30 patients were screened. In the end, all the patients who met the inclusion criteria were randomized into the study. Randomization was done using blind card selection method. Baseline details of all the patients were represented in Table 1. There was no statistical difference in the patient characteristics among the groups.

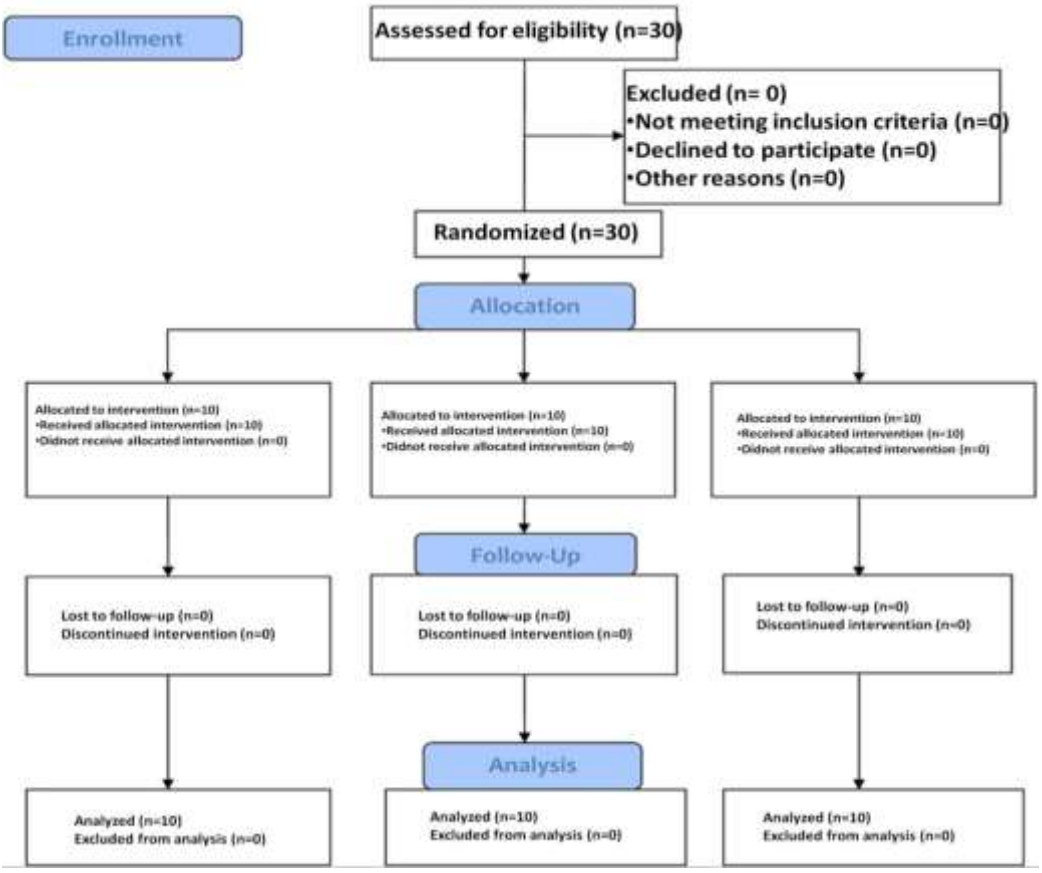

Figure 1: CONSORT Flow chart.

S.No	PATIENT CHARACTERISTICS		Group 1 (N=10)	Group 2 (N=10)	Group 3 (N=10)	P value
1	Age (Mean ± SD)		41.7±3.97	44.9±8.45	39.7±8.7	0.29#
2	Gender (N)	Male	7 (70%)	5 (50%)	7 (70%)	0.56*
		Female	3 (30%)	5 (50%)	3 (30%)	
3		Right	29.63±5.9	34.6±6.9	34.7±5.2	0.0001#
	Baseline IOP (mm Hg)	Left	30.31±4.9	34.7±6.2	35.4±4.6	
		Total	30.0±0.5	34.7±0.1	35.1±0.4	

Table 1: Patients demographic data. # P value obtained with ANOVA, * P value obtained with Chi-square test. N= number of patients.

Group 1 patients had a baseline IOP of 30.0±0.5 mm Hg. On day 3 of treatment, the IOP values significantly (P value-0.0001) improved to 25.8±0.3 mm Hg. Group 2 patients also showed improvement of IOP from baseline (34.7±0.1) to day 3 (28.5±0.1) treatment. Group 3 patients also had significant improvement of IOP from baseline (35.1±0.4) to day 3 (25.9±0.2). Comparing the efficacies of three groups on day 3, there was significant difference between the IOP of group 1 and group 2, but group 1 and group 3 IOP values were comparable [Figure 2].
The reduction of IOP was described in Figure 3 and percentage reduction in Figure 4. The reduction of IOP in group 1, 2, 3 patients on day 3 was 4.13±0.16 mm Hg, 6.18±0.04 mm Hg and 9.15±0.27 mm Hg respectively. The reduction was high in group 3 patients.

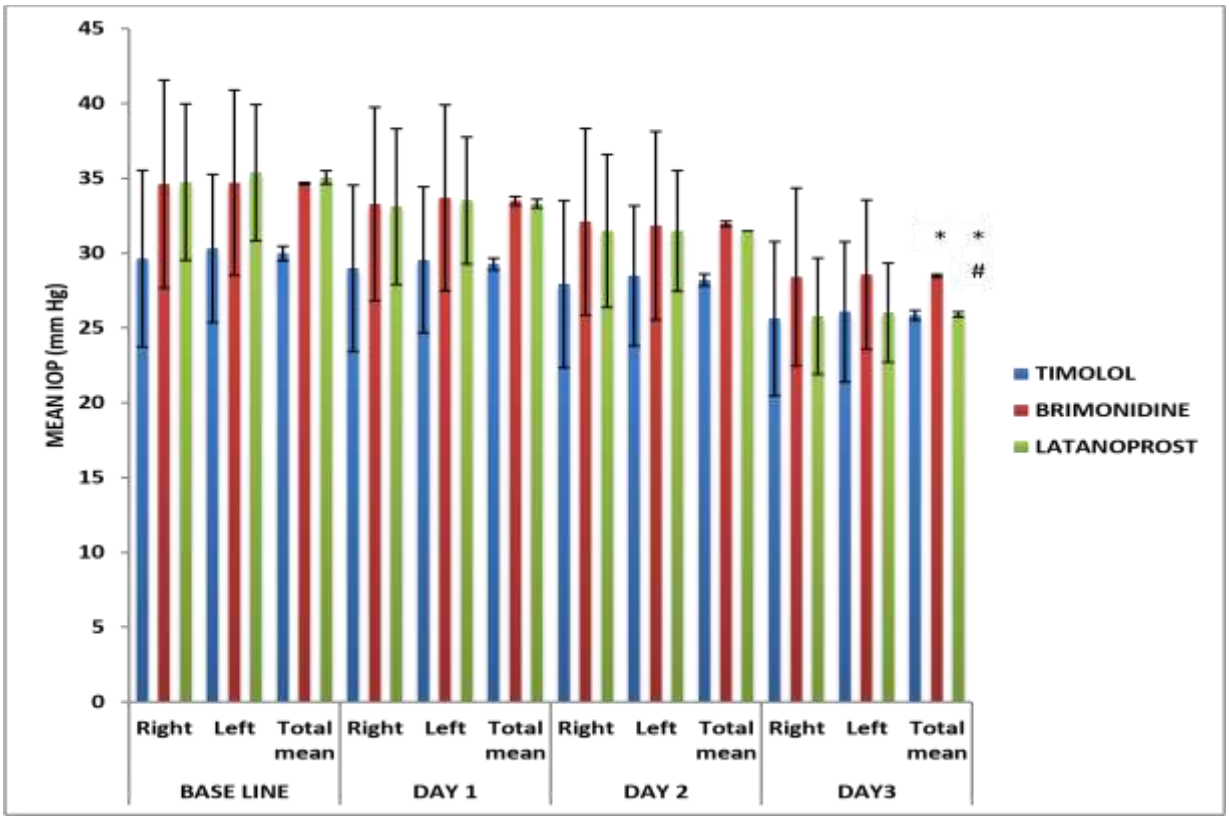

Figure 2: Effects of timolol, brimonidine and latanoprost on intraocular pressure. The values expressed in mean and standard deviations, IOP- intraocular pressure, * compared with baseline within group (p value <0.05), # compared between timolol and latanoprost (p value =0.4).

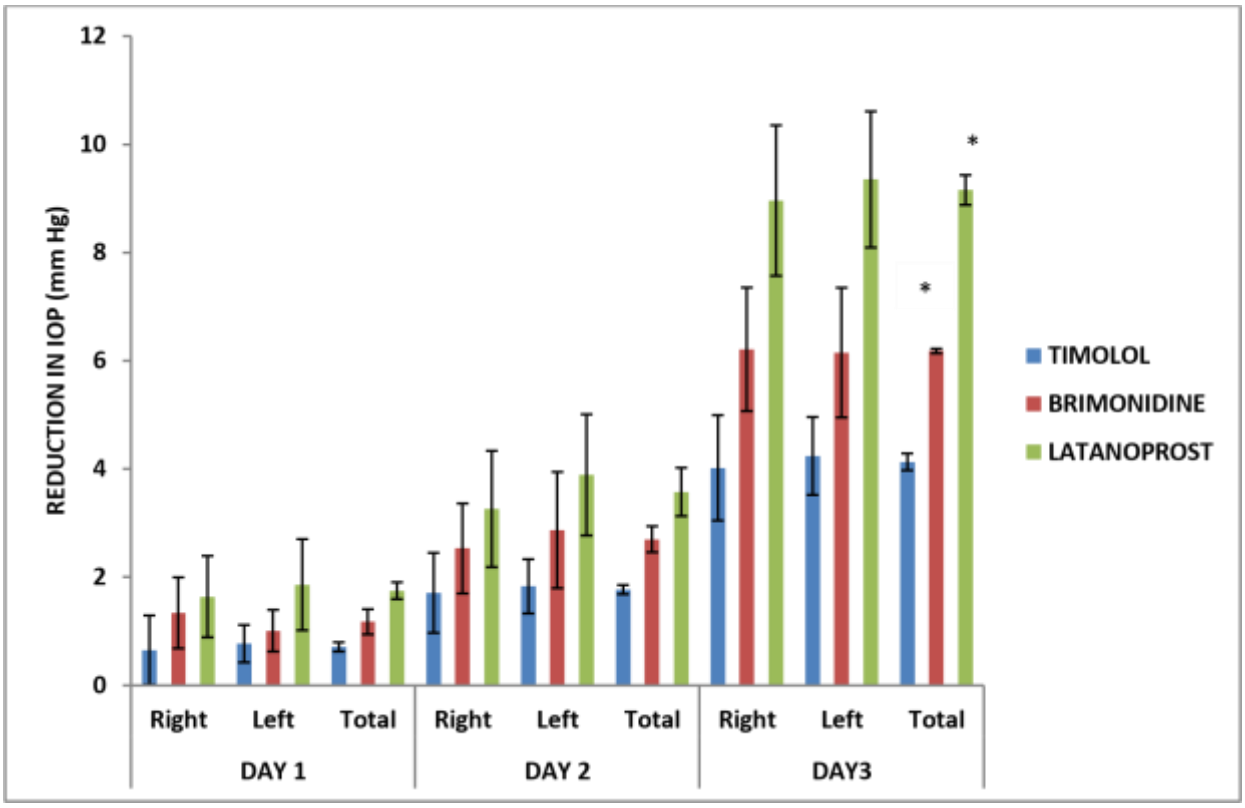

Figure 3: Effects of timolol, brimonidine and latanoprost on intraocular pressure reduction. The values expressed in mean and standard deviations, IOP- intraocular pressure, * compared with timolol (p value <0.05).

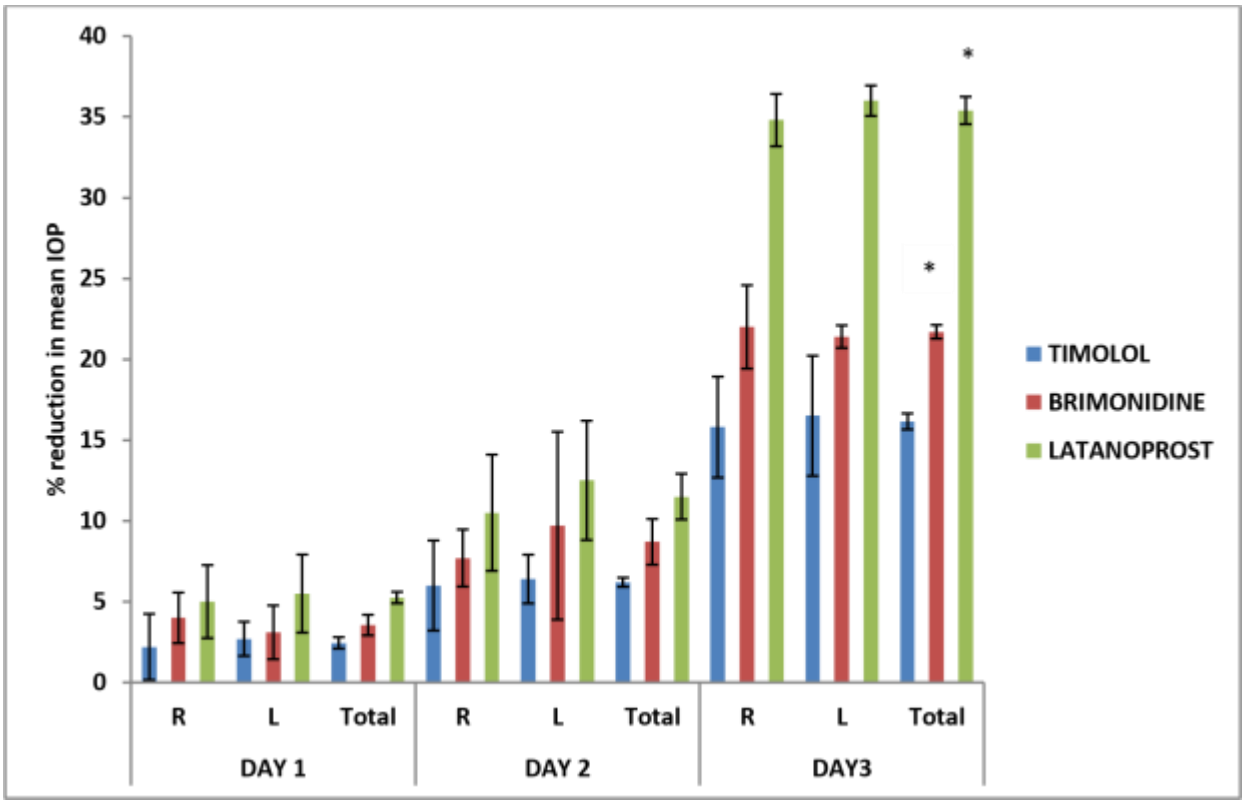

Figure 4: Effects of timolol, brimonidine and latanoprost on percentage reduction of intraocular pressure. The values expressed in mean and standard deviations, IOP- intraocular pressure, * compared with timolol (p value <0.05).

DISCUSSION

This is a prospective randomized, three-arm study. The objective of the present study is to evaluate the efficacy of Timolol (0.5%), Brimonidine (0.2%), Latanoprost (0.005%), in glaucoma patients. Latanoprost showed more efficacy in reducing the IOP when compared to other two drugs in the study. The decrease in mean IOP after topical administration of timolol (0.5), 4.0 mm Hg in right eye & 4.3 mm Hg in left eye, this was in agreement with previous study [9]. There is less decrease (6%) in IOP in this group of patients, this may be due to patients developing resistance towards timolol because of some of the patients are already on glaucoma treatment with timolol for a long period of time. Such changes in IOP reduction by timolol was reported by Javitt JC & Schiffman

RM (2000) [10]. However there is less decrease (2.1 mmHg) in the IOP as compared to our study. The decrease in the mean IOP after topical administration of Brimonidine (0.2%) was 6.2 mmHg in right eye & 6.1 mmHg in left eye, this was in agreement with R Thomas et al.,(2003) and Joel S. Schuman et al.,(1997) [11, 12]. In all the studies there was similar decrease in the IOP with brimonidine, this results shows, patients responded more effectively to brimonidine.

The decrease in the IOP after topical administration of Latanoprost (0.005%) was 9.0 mmHg in right eye & 9.3 mmHg in left eye, this was in agreement with Einarson et al.,(2000), whose study also demonstrated similar decrease in IOP [13]. Such changes in 1.0.P. reduction with Latanoprost
(0.005%), was also reported [14]. The order of effectiveness of the study drugs may be shown as Timolol < Brimonidine < latanoprost.

The present study was conducted in small group of patients, which may be considered as a limitation for this study. Further studies including larger sample size may be required to evaluate the effectiveness.

CONCLUSION

Timolol, brimonidine and latanoprost showed significant efficacy in decreasing IOP from baseline.
Latanoprost showed superior efficacy among the other two drugs, timolol and brimonidine.

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